HEALTHY BIRTH,
GROWTH & DEVELOPMENT

knowledge integration

BILL & MELINDA
GATES *foundation*

> "When mothers have healthy pregnancies, and when children thrive, the positive benefits last a lifetime."
> —MELINDA GATES

Parents are obsessed with measuring their children. We start when the baby is in utero: the size of a grain of rice, a grape, a lemon. When the baby is born, the key pieces of information we share are the name and 2 measurements: length and weight. Then we track length and weight compared to other children. Gradually, the milestones become more qualitative, but we don't stop measuring. "My child is smiling." "My child is walking." "My child is acting like a teenager."

Why do we measure? There are important practical reasons. Measurements provide an indication of our children's health. But the act of measuring also takes on an emotional resonance. Parents take great joy in watching their children grow. Each milestone reached seems to be a testament to their limitless potential.

But this is not how millions of people in poor countries experience parenting. They don't have

access to good enough health care to establish whether their children are growing and developing normally. If they did, in many cases they would find that their children are lagging. In poor countries, 1 in 10 babies is born preterm; 1 in 3 children falls off the standard physical growth curve; and more than 1 in 3 misses key behavioral milestones because the brain isn't developing properly.

In poor countries, children's potential doesn't seem quite so limitless. These children – and their communities – can be robbed of their future from the very beginning, and there is no way to get that future back.

In 2013, the Bill & Melinda Gates Foundation created the Healthy Birth, Growth, and Development program (HBGD) to ensure that all children can regain control of their futures, maximize their potential, and have the opportunity to lead a healthy and productive life.

15 MILLION CHILDREN ARE BORN EVERY YEAR BEFORE THEY REACH FULL TERM (PRETERM).

ABOUT 150 MILLION CHILDREN UNDER AGE 5 YEARS ARE STUNTED, OR SHORT FOR THEIR AGE.

THE BRAINS OF 200 MILLION CHILDREN UNDER AGE 5 YEARS DON'T DEVELOP NORMALLY.

HEALTHY BIRTH, GROWTH, & DEVELOPMENT

These numbers on the left are so high because these problems are complex and not well understood.

They are complex because so many factors affect how children grow and develop, each factor interacts with the others in dynamic ways, and the relations between the factors change depending on the circumstances.

There is no magic pill that we can invent to guarantee that children grow and develop as they should. Instead, healthy birth, growth, and development will require packages of interventions that address many factors simultaneously.

HBGD intends to fill the key knowledge gaps in the field that prevent us from knowing how to use our scarce resources to intervene effectively. HBGD is organized around a list of key questions, and the answers to these questions will help the foundation and its partners cut through some of the complexity and start to reduce the heavy burden of preterm birth, stunting, and neurocognitive impairment.

HBGD'S KEY QUESTIONS

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INTERACTION BETWEEN GROWTH & DEVELOPMENT OUTCOMES	Can we quantitatively characterize the relation and interaction between preterm birth, physical growth, and brain development?
GROWTH OUTCOMES DETERMINANTS	To what extent is growth faltering explained by pre- vs postnatal insults?
	What kind of recovery can we expect in infants born small for gestational age (SGA)?
PATHWAYS	Are there disproportionately large contributions to growth faltering from certain pathways, and can we rank-order risk factors?
	Are there specific pathways directly impacting linear growth faltering that coincide with increased risk of noncommunicable diseases such as cardiovascular disease, obesity, and diabetes?
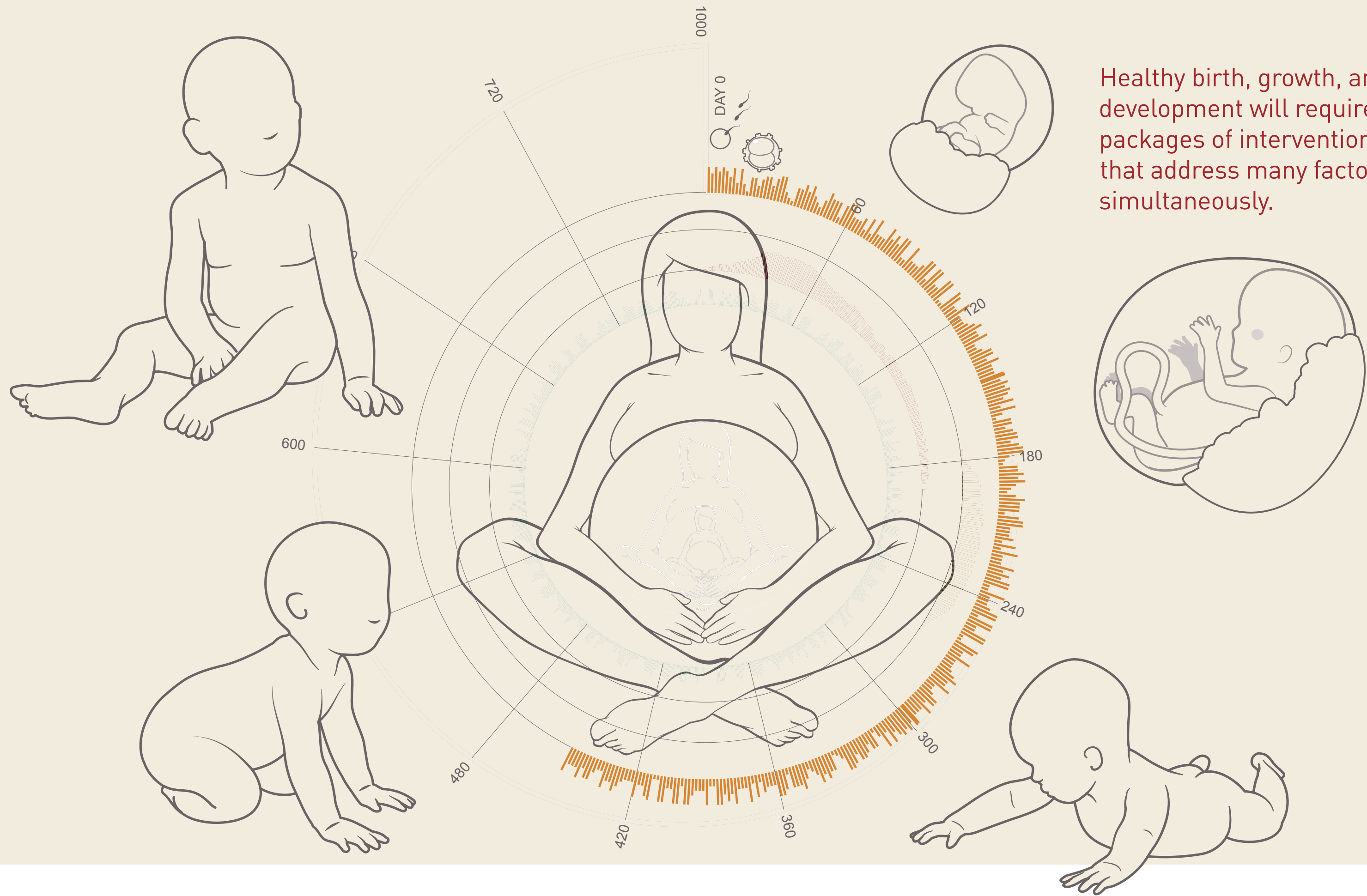
Healthy birth, growth, and development will require packages of interventions that address many factors simultaneously.

1000

DAY 0

720

60

120

600

180

240

480

300

420

360

HEALTHY BIRTH, GROWTH, & DEVELOPMENT
knowledge integration

Within HBGD, the knowledge integration initiative (HBGD*ki*) aims to answer the key questions by analyzing the large body of data that already exists.

Researchers have been studying birth, growth, and development for decades, but most of the data they've collected are stored on hard drives or in file cabinets where no one has access to them. HBGD*ki* has brought a lot of these data together into a large and diverse knowledge base. HBGD*ki* is visualizing and analyzing the data using state-of-the-art analysis methods and tools to generate new insights that will help us answer the key questions.

DATA, DISCOVERY, DECISIONS

DATA
HBGD*ki* has worked with researchers from around the world to get access to data from more than 120 observational studies and randomized controlled clinical trials representing almost 10 million children from 25 countries and almost 1900 variables. The knowledge base also includes census data and population surveys.

DISCOVERY
HBGD*ki* is using new modeling and visualization methods to understand and analyze the knowledge base. We take four different approaches to modeling.

Causal models describe cause and effect. For example, a causal model could aim to establish how a given intervention or combination of interventions affects physical growth or neurocognitive development.

Population models describe populations at large. For example, a population model could help us understand how the burden of disease is changing.

Empirical models help us make sense of data from studies by, for example, fitting a curve to the data to identify key trends, which we are then able to interpret. Empirical models, based on observed data, are distinct from theoretical models that assume certain conditions.

Mechanistic models see an underlying biological mechanism that's relevant to the outcome we're trying to understand. So, HBGD*ki* data analysts are building a model of the human gut using mathematical equations to see how it processes nutrients, and to start drawing conclusions about how this process impacts physical growth and neurocognitive development.
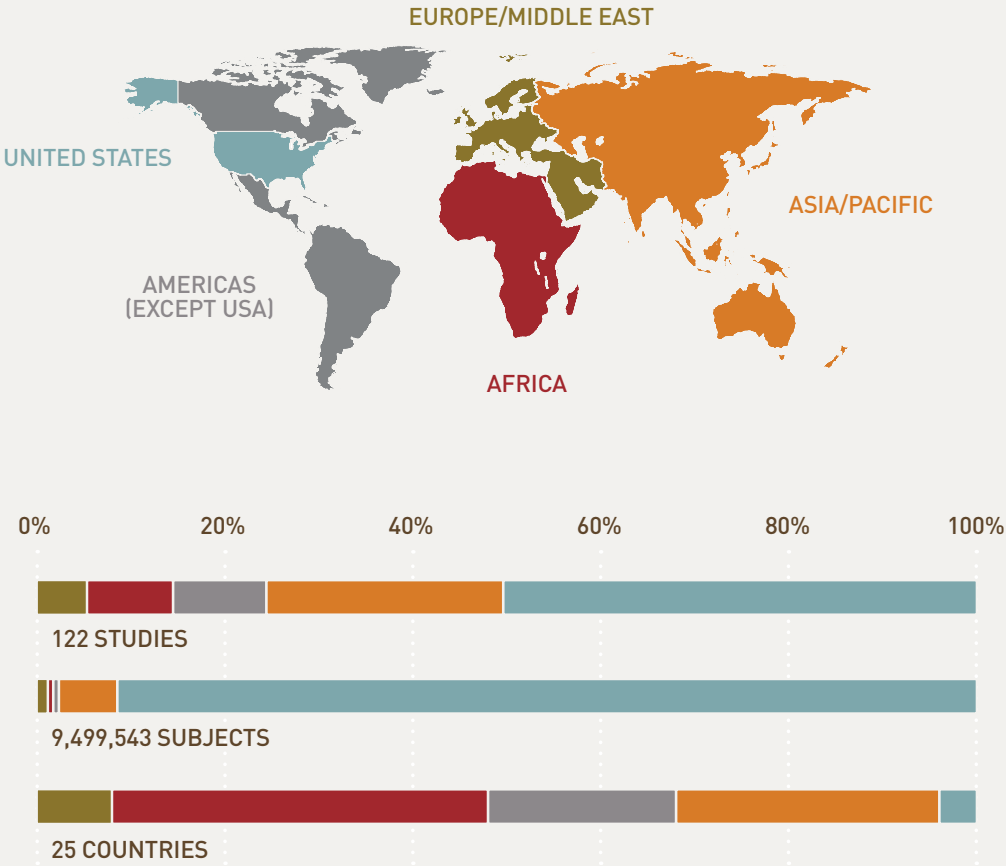
DECISIONS
The data and discovery processes are geared toward informing decisions about how the foundation and the larger global health community can use limited resources to have the greatest impact on children's lives.

The ultimate goal, as stated by the foundation's CEO, Sue Desmond-Hellmann, is "precision public health"—that is, replacing one-size-fits-all solutions with customized solutions that deliver the right interventions to the right child at the right times.

By gathering enough data and analyzing them at a high enough resolution, we can start to organize children into clinically coherent groups, predict the risks each group faces, and design interventions to limit those risks.

This new approach to global public health relies on the kind of detailed insights that HBGD*ki* is designed to generate.

HBGD*ki* KNOWLEDGE BASE

EUROPE/MIDDLE EAST

UNITED STATES

ASIA/PACIFIC

AMERICAS (EXCEPT USA)

AFRICA

| 0% | 20% | 40% | 60% | 80% | 100% |

122 STUDIES

9,499,543 SUBJECTS

25 COUNTRIES

DATA MANAGEMENT & VISUALIZATION

The Data Management & Visualization surge team is the vital interface between data sources and analytics communities, and aims to reduce time to early insights by curating analysis data sets with state-of-the-art common data specification, security, and quality standards.

OPEN INNOVATION

The Open Innovation surge team mobilizes the global "unusual suspects" data science network to collectively extract and evolve novel insights from large complex data streams, and to harness innovation inherent in the collective community.

QUANTITATIVE PHYSIOLOGIC MODELING

The Quantitative Physiologic Modeling (qPM) surge team aims to develop an in silico, systems physiology, and integrative framework to quantitatively characterize interactions of nutrients (quantity and quality), gut function, infectious and noninfectious microbes, environmental enteropathy pathways, and other risk factors that impact birth, somatic growth, and neuro-developmental outcomes.

SUPER LEARNER & CAUSAL MODELING

The Super Learner team is using machine learning and targeted learning to address substantive research questions related to the goals of HBGD*ki*, while demonstrating the statistical benefits of the targeted learning approach.

HIGH RISK, POTENTIAL HIGH REWARD

Supports exceptionally bold and creative data science initiatives with broad potential impact to promote healthy birth, growth, and development in the communities that need it most.

POLICY, DELIVERY, & IMPLEMENTATION

The Policy, Delivery, & Implementation surge team aims to analyze growth and development outcomes across geographic, regional, cultural, and socioeconomic trends that contribute to poor growth outcomes, and to support our ability to promote healthy birth, growth, and development in the communities that need it most by delivering the right interventions to the right child, at the right time, and at the right price.

LIFECYCLE, AUXOLOGY, & NEUROCOGNITIVE DEVELOPMENT

The Lifecycle, Auxology, & Neurocognitive Development surge team strives to increase the understanding of variability in sensitivity, intensity, and duration of growth faltering resulting from insults, and to optimize the capacity for targeted interventions to promote recovery during critical growth and development periods from conception to reproductive age across generations.

FETAL GROWTH, PREGNANCY, & NEWBORN OUTCOMES

The Fetal Growth, Pregnancy, & Newborn Outcomes surge team seeks to quantitatively characterize evolving interactions between maternal and fetal factors that drive fetal development, pregnancy and newborn outcomes, and postnatal growth and development for preterm and term births.

KNOWLEDGE TRANSLATION

The Knowledge Translation surge team translates HBGD*ki* modeling, learning, and knowledge generation by transforming data to simple, understandable insights that drive action.

> "The innovations of tomorrow depend on the opportunities available to children today."
>
> —BILL GATES

◄ HBGD*ki* IN ACTION
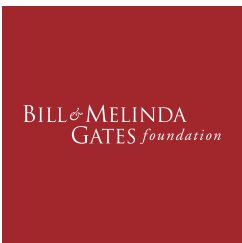
The HBGD*ki* team includes more than 150 people:

Principal investigators who contribute data to the knowledge base, and advise the analysts about how to interpret the data.

Data analysts, modelers, and visualization experts who are working with the knowledge base.

Gates Foundation staff who provide global health expertise and collaborate with the analysts to create strategies for answering key questions.

The analyses will be ongoing through 2017. HBGD*ki* is using the insights from analysis results and data visualizations to recommend better grant making, public policy, and clinical practice.

The end result will be a world with fewer children who have preterm birth, stunting, or neurocognitive impairment. More children will have the chance to lead healthy and productive lives, and more parents will eagerly measure their children's progress toward a thriving future.